REMARKS

I. Status of the Claims

Claims 1-20 were originally filed. Subsequently, claims 3-20 were canceled and new claim 21 was added.

Upon entry of the present amendment, claim 1 is amended to recite "being encoded by a nucleic acid capable of under stringent hybridization conditions specifically hybridizing to a polynucleotide sequence, the antisense sequence of the polynucleotide sequence encoding the amino acid sequence of SEQ ID NO:2" and the stringent hybridization conditions, which find support in the specification, *e.g.*, on page 12, lines 12-21, and page 13, lines 13-30. Claim 2 is amended to improve clarity of the claim language. New claims 22 and 23 are added and recite a polynucleotide sequence set forth in SEQ ID NO:1, which also finds support throughout the specification (*e.g.*, on page 3, lines 13-16, and in Example 2 on page 38). No new matter is introduced.

II. Claim Rejections

A. 35 U.S.C. §112, First Paragraph: Written Description

The Examiner sustained the rejection of claim 1 under 35 U.S.C. §112, first paragraph, for alleged inadequate written description of the claimed subject matter so as to reasonably convey to one of skill in the art that the inventors, at the time of filing, had possession of the claimed invention. Applicants respectfully traverse this rejection for reasons previously stated. To expedite prosecution, however, claim 1 has been amended to structurally define the claimed polypeptide based on its coding polynucleotide sequence. The written description rejection is addressed to the extent that it may apply to the amended claims.

Possession of claimed invention may be shown by a variety of descriptive means, including words, structure, figures, diagrams, and formulas. MPEP §2163 I. Case law provides more specific guidance in setting the standard for written description.

Claim 1 as amended is directed to an isolated ATP-binding cassette protein having the following properties: (i) conferring mitoxantrone resistance to S1-M1-80 human colon carcinoma cells when expressed in the cells; (ii) being encoded by a nucleic acid capable of under stringent hybridization conditions specifically hybridizing to a polynucleotide sequence, the antisense sequence of which encodes the amino acid sequence of SEQ ID NO:2, wherein the stringent hybridization conditions comprise a sodium ion concentration of from about 0.01 to about 1.0 M, a pH of from about 7.0 to about 8.3, and a temperature of about 60°C; and (iii) having a molecular weight between about 70 kDa and about 75 kDa. This claim fully complies with the requirements for written description of a chemical genus as set forth in *University of California v. Eli Lilly & Co.*, 43 USPQ2d 1398 (Fed. Cir. 1997).

As described by the Federal Circuit in *Lilly*, "[a] description of a genus of cDNAs may be achieved by means of . . . a recitation of structural features common to the members of the genus . . . ." *Lilly*, 43 USPQ2d at 1406. Furthermore, the court in *Fiers v. Revel* stated that an adequate written description "requires a precise definition, such as by structure, formula, chemical name, or physical properties." *Fiers*, 25 USPQ2d 1601, 1606 (Fed. Cir. 1993).

Besides defining the structural features of a claimed invention, proper description of functional features of the invention can also play an important role in satisfying the written description requirement. The Federal Circuit recently stated that "*Lilly* did not hold that all functional descriptions of genetic material necessarily fail as a matter of law to meet the written description requirement; rather, the requirement may be satisfied if in the knowledge of the art the disclosed function is sufficiently correlated to a particular, known structure." *Amgen Inc. v. Hoechst Marion Roussel Inc.*, 65 USPQ2d 1385, 1398 (Fed. Cir. 2003).

With regard to the claimed polypeptides, claim 1 sets forth both functional features, *e.g.*, conferring mitoxantrone resistance to S1-M1-80 human colon carcinoma cells when expressed in the cells, and structural features, *e.g.*, being encoded by a nucleic acid capable of specifically hybridizing, under specified conditions, to a polynucleotide sequence that complements the sequence encoding the amino acid sequence of SEQ ID NO:2.

The ability for a nucleic acid to hybridize under given conditions to a reference polynucleotide sequence, such as a DNA sequence encoding a particular amino acid sequence, is a physical/structural property of the nucleic acid, because it relies upon the nucleotide sequence of the molecule. *See, e.g.*, Sambrook et al., *Molecular Cloning: A Laboratory Manual*, pages 9.47-9.51 (2nd ed. 1989), attached as **Exhibit A**; Stryer, *Biochemistry*, pages 80-82 (3rd ed. 1988), attached as **Exhibit B**. This physical/structural property of the nucleic acid in turn becomes a physical/structural property of the polypeptide encoded by the nucleic acid, since the amino acid sequence of the polypeptide is determined by the nucleotide sequence of the nucleic acid. As described in Stryer, the transition between hybridization and melting of complementary nucleic acid strands is abrupt and largely sequence dependent. When the temperature of hybridization is provided, one of skill in the art would be able to predict whether or not a given sequence would hybridize to a reference sequence (*see, e.g.*, equations provided in Sambrook, *supra*). Thus, pending claims set forth commonly shared structural features of the claimed polypeptides via defining their coding sequences. As such, by reciting the specific hybridization under stringent conditions between the polynucleotide sequences encoding the claimed polypeptides and a reference nucleic acid encoding the amino acid sequence of SEQ ID NO:2, the pending claims set forth commonly shared structural features of the claimed genus of polypeptides.

On the other hand, commonly shared functional feature of the claimed genus of polypeptides is also provided: each is capable of conferring mitoxantrone resistance to S1-M1-80 human colon carcinoma cells when expressed in the cells. This functional feature can be readily tested by one of ordinary skill in the art using well established, routinely practiced techniques as well as according to the teaching of the present specification (*see, e.g.*, page 35 line 24 to page 37 line 2 and Example 3 on page 38).

Thus, both structural and functional features commonly shared by the claimed genus have been described in detail, which "clearly allow persons of ordinary skill in the art to recognize that [the applicant] invented what is claimed." *Vas-Cath Inc. v. Mahurkar*, 19 USPQ2d 1111, 1116 (Fed. Cir. 1991). Such description is consistent with the standards set forth

in both *Lilly* and *Amgen*. Applicants therefore believe that the claimed invention within the current claim scope is properly described by the specification under 35 U.S.C. §112, first paragraph. The withdrawal of the written description rejection is respectfully requested.

B. 35 U.S.C. §102: Anticipation

The Examiner also maintained the rejection of claims 1 and 2 under 35 U.S.C. §102(a) for alleged anticipation by the Doyle *et al.* reference and the rejection of claims 1 and 2 under 35 U.S.C. §102(e) for alleged anticipation by U.S. Patent No. 6,313,277 to Ross *et al.* Applicants respectfully traverse the rejection.

To swear behind Doyle *et al.* and Ross *et al.* (which have effective dates of Feb. 5, 1998, or later), Applicants submitted the Declaration of Drs. Michael Dean, Rando Allikmets, Susan Bates, and Antonio Fojo under 37 C.F.R. §1.131 ("the Declaration"), which the Examiner has acknowledged shows that Applicants had possession of SEQ ID NOs:1 and 2 prior to Feb. 5, 1998 (Final Office Action of March 17, 2004, last paragraph on page 3). The Examiner asserted, however, that the Declaration has failed to swear behind the two cited references because the references disclose sequences 99.4% and 99.8% but not 100% identical to SEQ ID NO:2. The Examiner's position is inconsistent with the standards set forth in the MPEP.

According to MPEP §715.02,

> [A] 37 CFR 1.131 affidavit is not insufficient merely because it does not show the identical disclosure of the reference(s) or the identical subject matter involved in the activity relied upon. If the affidavit contains facts showing a completion of the invention commensurate with the extent of the invention as claimed is shown in the reference or activity, the affidavit or declaration is sufficient, whether or not it is a showing of the identical disclosure of the reference of the identical subject matter involved in the activity.

This section of the MPEP describes precisely the situation of the present case. This application relates to novel ATP-binding cassette (ABC) proteins that confer cytotoxicity resistance to cancer cells. The specification identifies, among other things, the polynucleotide sequence (SEQ ID NO:1) and the amino acid sequence (SEQ ID NO:2) of a full length ABC

protein. In addition to various methods and techniques well known in the art of molecular and cellular biology, the specification teaches how to make variants of the exemplary ABC proteins and confirm their retained functionality. See, *e.g.*, description of amino acid conservative substitution is provided in the specification on page 14, line 14, to page 15, line 3; assays for mitoxantrone resistance are described on page 35, line 22, to page 37, line 2, and in Example 3 on pages 38-39. Thus, the identification of SEQ ID NOs:1 and 2 combined with the general knowledge of an artisan is not only commensurate with but even beyond the extent of the invention as shown in the two cited references. By showing that the present inventors took possession of SEQ ID NOs:1 and 2 prior to the critical date of Feb. 5, 1998, the Declaration has in essence established the inventors' possession before that date of a genus of ABC proteins with the function of conferring mitoxantrone resistance to cancer cells, as defined by the currently pending claims.

As such, Applicants submit that the Doyle *et al.* reference and the Ross patent are not available as prior art references under 35 U.S.C. §102(a) or §102(e). Accordingly, the withdrawal of the anticipation rejections is respectfully requested.

CONCLUSION

In view of the foregoing, Applicants believe all claims now pending in this Application are in condition for allowance. The issuance of a formal Notice of Allowance at an early date is respectfully requested.

If the Examiner believes a telephone conference would expedite prosecution of this application, please telephone the undersigned at 415-576-0200.

Respectfully submitted,

Chuan Gao
Reg. No. 54,111

TOWNSEND and TOWNSEND and CREW LLP
Two Embarcadero Center, Eighth Floor
San Francisco, California 94111-3834
Tel: 415-576-0200
Fax: 415-576-0300

Attachments (**Exhibit A**: Sambrook *et al.*; and **Exhibit B**, Stryer)
CG:cg
60214395 v1